

Attorney Docket No.: **ISPH-0500**
Inventors: **Yu et al.**
Serial No.: **09/705,587**
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- SubDI
- a) preparing a bodily fluid or extract for analytical detection to form a liquid sample;
- b) contacting said liquid sample with a probe complementary to an oligonucleotide so that the probe and the oligonucleotide can form hybrid moieties in said liquid sample, wherein said probe comprises a detectable marker and a binding moiety;
- c) placing said liquid sample in contact with a solid support to which a binding partner of said binding moiety is attached so that said hybrid moieties present in said liquid sample will be attached to said solid support;
- d) removing any oligonucleotide from said liquid sample that has not formed a hybrid moiety;
- e) contacting said liquid sample with a single strand oligonucleotide-specific nuclease under conditions in which probe which is not hybridized to form said double-stranded oligonucleotide moieties hybrid moieties is degraded and thus is no longer attached to said solid support;
- f) removing any unbound detectable marker from said liquid sample; and
- g) detecting a label associated with said marker wherein the presence of said label indicates the presence of said hybrid moieties bound to said solid support wherein detection of said
- C'

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Sub D1 label at levels above the level characteristic of a liquid sample that was prepared as a blank sample to contain no oligonucleotide indicates the presence of said oligonucleotide in said liquid sample.

C' 14. The method of claim 13, wherein said bodily fluid is plasma.

Sub D2 15. The method of claims 13, wherein said oligonucleotide comprises at least one phosphorothioate linkage.

16. The method of claim 13, wherein said oligonucleotide comprises a modification at the 2' position of at least one sugar moiety.

17. The method of claim 16, wherein said 2' modification is a 2'-O-methoxyethyl modification.

Sub D3 18. The method of claim 13, wherein said oligonucleotide comprises at least one modified base.

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19. The method of claim 18, wherein said modified base is 5-methylcytosine.

Cⁱ
20. The method of claim 13, wherein said marker is digoxigenin.

21. The method of claim 13, wherein said label is a colorimetric, radioactive, chemiluminescent, enzymatic or fluorescent label.

22. The method of claim 13, wherein said single-strand specific nuclease is S1 nuclease or mung bean nuclease.--

REMARKS

Claims 1-10 and 12 are pending in this application. Claims 1-10 and 12 have been canceled. New claims 13-22 have been added to incorporate subject matter of the canceled claims and to clarify the instant invention. Support for these new claims can be found throughout the specification as filed.